```
FILE 'REGISTRY' ENTERED AT 09:56:32 ON 18 NOV 2002

=> S URICASE/CN
L1             1 URICASE/CN

=> D

L1   ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2002 ACS
RN   9002-12-4  REGISTRY
CN   Oxidase, urate (9CI)  (CA INDEX NAME)
OTHER NAMES:
CN   E.C. 1.7.3.3
CN   Urate oxidase
CN   Urate: O2-oxidoreductase
CN   Uratoxidase
CN   Uric acid oxidase
CN     ***Uricase***
CN   Uricozyme
MF   Unspecified
CI   MAN
LC   STN Files:   ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, BIOBUSINESS,
       BIOSIS, BIOTECHNO, CA, CAPLUS, CBNB, CHEMCATS, CHEMLIST, CIN, CSCHEM,
       DDFU, DRUGU, EMBASE, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, PHAR,
       PROMT, RTECS*, TOXCENTER, USPAT2, USPATFULL
         (*File contains numerically searchable property data)
     Other Sources:   EINECS**, TSCA**
         (**Enter CHEMLIST File for up-to-date regulatory information)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
            1566 REFERENCES IN FILE CA (1962 TO DATE)
              67 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
            1568 REFERENCES IN FILE CAPLUS (1962 TO DATE)


FILE 'CAPLUS' ENTERED AT 09:56:56 ON 18 NOV 2002

=> S URICASE OR L1
          1921 URICASE
            27 URICASES
          1925 URICASE
                 (URICASE OR URICASES)
          1568 L1
L2        2433 URICASE OR L1

=> S POLYETHYLENE GYCOL;S PEG
        281468 POLYETHYLENE
          9136 POLYETHYLENES
        284121 POLYETHYLENE
                 (POLYETHYLENE OR POLYETHYLENES)
            40 GYCOL
             4 GYCOLS
            44 GYCOL
                 (GYCOL OR GYCOLS)
L3           6 POLYETHYLENE GYCOL
                 (POLYETHYLENE(W)GYCOL)


         24110 PEG
           881 PEGS
L4       24498 PEG
                 (PEG OR PEGS)

=> S POLYETHYLENEGYCOL
L5           3 POLYETHYLENEGYCOL

=> S POLYETHYLENE GLYCOL;S PEG
        281468 POLYETHYLENE
          9136 POLYETHYLENES
        284121 POLYETHYLENE
                 (POLYETHYLENE OR POLYETHYLENES)
        286141 GLYCOL
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      36965 GLYCOLS
     299216 GLYCOL
            (GLYCOL OR GLYCOLS)
L6    77344 POLYETHYLENE GLYCOL
            (POLYETHYLENE(W)GLYCOL)


      24110 PEG
        881 PEGS
L7    24498 PEG
            (PEG OR PEGS)

=> S L6,L7
L8    91015 (L6 OR L7)

=> S L8 (W) (10000 OR 10);S L8 (W) (20000 OR 20);S L8 (W) (25000 OR 25);S L8 (W) (30000 OR 30)
       3647 10000
    3245741 10
L9      370 L8 (W) (10000 OR 10)


       1379 20000
    1970480 20
L10     685 L8 (W) (20000 OR 20)


        622 25000
    1275324 25
L11      66 L8 (W) (25000 OR 25)


        709 30000
    1602386 30
L12     138 L8 (W) (30000 OR 30)

=> S L9 AND L2;S L10 AND 23;S L11 AND L2;S L12 AND L2
L13      2 L9 AND L2


     370657 23
L14      12 L10 AND 23


L15       0 L11 AND L2


L16       0 L12 AND L2

=> S L13,L14
L17      14 (L13 OR L14)

=> D 1-14 CBIB ABS

L17  ANSWER 1 OF 14  CAPLUS  COPYRIGHT 2002 ACS
2002:428743  Document No. 136:406908  Pharmaceutical formulations comprising
     paclitaxel and solubilizers.  Chen, Hongming (Transform Pharmaceuticals,
     Inc., USA).  PCT Int. Appl. WO 2002043765 A2 20020606, 69 pp.  DESIGNATED
     STATES: W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH,
     CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM,
     HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU,
     LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD,
     SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW,
     AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI,
     CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL,
     PT, SE, SN, TD, TG, TR.  (English).  CODEN: PIXXD2.  APPLICATION: WO
     2001-US43306 20011120.  PRIORITY: US 2000-PV253640 20001128; US
     2001-PV272117 20010228.
AB   The invention concerns paclitaxel solubilizers and formulations thereof
     with a high propensity to dissolve paclitaxel.  The formulations of the
     invention reduce or obviate the need for the disadvantageous excipient
     Cremophor EL.  The formulations of the invention are suitable for
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parenteral, oral, local, or transdermal administration to mammals including humans, particularly for i.v. delivery. Formulations contained, e.g., paclitaxel ***PEG*** ***20*** glyceryl monooleate, ethanol, Polysorbate 80, benzethonium chloride and citric acid.

L17 ANSWER 2 OF 14 CAPLUS COPYRIGHT 2002 ACS
2001:417471 Document No. 135:142105 Immunological Properties of ***Uricase*** Conjugated to Neutral Soluble Polymers. Caliceti, Paolo; Schiavon, Oddone; Veronese, Francesco M. (Department of Pharmaceutical Sciences, University of Padua, Padua, Italy). Bioconjugate Chemistry, 12(4), 515-522 (English) 2001. CODEN: BCCHES. ISSN: 1043-1802. Publisher: American Chemical Society.

AB For a comparative study of immunol. properties of protein-polymer conjugates, ***uricase*** was modified with poly(N-vinylpyrrolidone) 6000, poly(N-acryloylmorpholine) 6000, (c) branched monomethoxy ***polyethylene*** ***glycol*** ***10*** ,000, and (d) linear monomethoxy polyethylene glycol 5000 Da. Spectroscopic studies performed by UV, fluorescence, and CD did not show any relevant difference in protein conformation among the native and the conjugates. Immunol. studies showed that both ***uricase*** antigenicity and immunogenicity were altered by polymer conjugation to an extent that depended upon the polymer compn.; in particular, monomethoxypolyethylene glycol 10,000 Da remarkably reduced the protein antigenicity, while unexpectedly, the poly(N-vinylpyrrolidone) deriv. presented higher antigenicity than the native protein. In Balb/c mice, the native protein elicited a rapid and intense immunoresponse whereas all the conjugates induced a lower prodn. of anti-native ***uricase*** antibodies. The rank order of immunogenicity was native ***uricase*** > ***uricase*** -poly(N-vinylpyrrolidone) .gtoreq. ***uricase*** -poly(N-acryloylmorpholine) > ***uricase*** -monomethoxy polyethylene glycol 5000 Da > ***uricase*** -monomethoxy ***polyethylene*** ***glycol*** ***10000*** Da. The 4 conjugates also induced anti-polymer immunoresponse. Anti poly(N-vinylpyrrolidone) and anti poly(N-acryloylmorpholine) antibodies were generated from the first immunization, while low levels of anti-polymer antibodies were found with both polyethylene glycol conjugates only after the second immunization.

L17 ANSWER 3 OF 14 CAPLUS COPYRIGHT 2002 ACS
2000:201061 Document No. 132:241696 Water and oil emulsion solid cosmetic composition. Kellner, David Martin; Russ, Julio Gans; Sandewicz, Ida Marie; Shandler, Robin Felice; Wang, Tian Xiang (Revlon Consumer Products Corporation, USA). U.S. US 6042815 A 20000328, 14 pp. (English). CODEN: USXXAM. APPLICATION: US 1998-175941 19981021.

AB A water and oil emulsion solid cosmetic compn. comprises 0.1-20 % of a primary soap-based gelling agent, 0.01-20 % of a secondary gelling agent selected from the group consisting of an aq. phase gelling agent, an oil phase gelling agent; and mixts. thereof, 0.1-30 % emollient oil, 0.1-20 % surfactant, 0.1-50 % particulates having a particle size of 0.5 to 100 .mu.m, and 5-95% water. The compn. is moisturizing, provides a cool feel on application, and a smooth finish on the skin. An oil-in-water emulsion stick makeup contained dimethicone 12.44, titania 4.8, polyglyceryl-6-polyricinoleate 0.39, aluminum stearate 0.62, cyclomethicone 3.51, propylparaben 0.1, iron oxide yellow 1.0, iron oxide red 0.2, iron oxide black 0.08, talc 0.85, nylon-12 0.25, synthetic wax 1.5, isostearyl alc. 5.7, hydrogenated castor oil 1.5, water 41.03, ascorbic acid 0.1, sodium stearate 7.55, butylene glycol 13, methylparaben 0.3, ***PEG*** - ***20*** Me glucose sesquiisostearate 3.49, casein/carrageenan complex 0.96, CaCl2 soln. (10 %) 0. ***23*** , phenoxyethanol 0.5, tocopheryl acetate 0.1, retinyl palmitate 0.1, and ethylene brassylate 0.15 %.

L17 ANSWER 4 OF 14 CAPLUS COPYRIGHT 2002 ACS
2000:64895 Document No. 133:8853 Final report on the safety assessment of Ceteareth-2, -3, -4, -5, -6, -7, -8, -9, -10, -11, -12, -13, -14, -15, -16, -17, -18, -20, -22, - ***23*** , -24, -25, -27, -28, -29, -30, -33, -34, -40, -50, -55, -60, -80, and -100. Madhavan, Bindu Nair (USA). International Journal of Toxicology, 18(Suppl. 3), 41-49 (English) 1999. CODEN: IJTOFN. ISSN: 1091-5818. Publisher: Taylor & Francis Ltd..

AB Ceteareths, used in a large no. of cosmetics as surfactants, are the PEG ethers of cetearyl alc. To supplement the limited available data on Ceteareth compds., previous findings from the safety assessment of PEG,

several fatty alcs. (cetearyl alc., cetyl alc., and stearyl alc.), and Steareth compds. were considered. These data indicate little evidence of toxicity. Although various metabolites of monoalkyl ethers of ethylene glycol are reproductive and developmental toxins, given the methods of manuf. of Ceteareth compds., there is no likelihood of such compds. being present as impurities. Further, there would be only limited ethylene glycol monomer linked by an ether group to the Ceteareth moiety for the PEG-5 compds., little for the PEG-10 compds., and virtually none for the ***PEG*** - ***20*** and higher compds. Even if linked to ethylene glycol monomer, it was considered unlikely that the Ceteareth moieties would be metabolized (e.g., via .beta.-oxidn.) to simple Me, Et, Pr, or Bu groups. As the current data indicate, such short alkyl chains are needed in order for the prodn. of toxic alc. or aldehyde dehydrogenase metabolites. For longer alkyl chains there is evidence of diminishing toxicity, and extrapolation to much longer chains such as expected in the Ceteareth moieties suggests that there is no reproductive or developmental hazard posed by these Ceteareth compds. The principal clin. finding related to PEGs is based on data in bum patients- PEGs were mild irritants/sensitizers and there was evidence of nephrotoxicity. No such effects were seen in animal studies on intact skin. Cosmetic manufacturers should adjust product formulations contg. PEG to minimize any untoward effects when products are used on damaged skin. In the absence of specific impurities data, the possible presence of 1,4-dioxane and ethylene oxide impurities was of concern. The importance of using the necessary purifn. procedures to remove these impurities was stressed. Creams contg. Ceteareth-20 enhanced drug absorption. Ceteareth-15 (10% in formulation) was minimally irritating to rabbits after a single dermal exposure. In ocular studies, ethoxylated cetearyl alc. soln. was a severe irritant to unrinsed rabbit eyes and moderately irritating to rinsed eyes. In clin. studies, Ceteareth-15 (1.5% in formulation) produced minimal irritation when tested in both a 4- and 21-day patch test, and was not a sensitizer when tested (1.35% in formulation) in a repeat-insult patch test. Based on the limited data on Ceteareth compds. and the extensive data on chem. related ingredients, it was concluded that these ingredients are safe as used in cosmetic formulations. These ingredients, however, should not be used on damaged skin.

L17 ANSWER 5 OF 14 CAPLUS COPYRIGHT 2002 ACS

2000:34552 Document No. 132:83401 Composition for topical application containing a lipase, vitamin precursor and a fatty alcohol. Boussouira, Boudiaf; Pham, Dang-Man (L'Oreal, Fr.). Eur. Pat. Appl. EP 970691 A1 20000112, 12 pp. DESIGNATED STATES: R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO. (French). CODEN: EPXXDW. APPLICATION: EP 1999-401522 19990618. PRIORITY: FR 1998-8615 19980706.

AB Cosmetic compns. contain an enzyme such as lipase, a vitamin precursor such as a vitamin ester, and a C6-22 fatty alc. in which the ratio of the alc. to the vitamin precursor is 0.25-30:1. Thus, 0.1% retinyl palmitate was hydrolyzed by 94% in presence of 0.1% lipase and 0.1% steryl alc. as compared with ***23*** % for the control. An antiwrinkle cream contained Hostacerin CG 5, stearyl alc. 1.5, vaseline 2, mineral oil 4, dimethicone 3, cyclomethicone 3, dimethicone copolyol 1, triclosan 0.1, retinyl palmitate 1, propylene glycol 2, ***PEG*** - ***20*** 1, Lipolase 100L 1, phenoxyethanol 0.4, and water q.s. 100%.

L17 ANSWER 6 OF 14 CAPLUS COPYRIGHT 2002 ACS

1995:865306 Document No. 123:308967 Measurement of thermodynamic nonideality arising from volume-exclusion interactions between proteins and polymers. Wills, Peter R.; Georgalis, Yannis; Dijk, Jan; Winzor, Donald J. (Department of Physics, University of Auckland, Private Bag 92019, Auckland, N. Z.). Biophysical Chemistry, 57(1), 37-46 (English) 1995. CODEN: BICIAZ. ISSN: 0301-4622. Publisher: Elsevier.

AB The effective thermodn. radii of ***23*** ribosomal proteins from the 50 S subunit have been detd. by gel chromatog. on Sephadex G-50, thereby supporting the contention that most of the proteins of the 50 S ribosomal unit exhibit reasonably globular structures. To investigate further the usefulness of modeling proteins as spheres, the second virial coeff. describing excluded vol. interactions of some ribosomal proteins with two inert polymers, polyethylene glycol (PEG) and dextran, has been detd. by gel chromatog. and/or sedimentation equil. techniques. Protein-polymer excluded vols. obtained with ***PEG*** ***20*** ,000 and Dextran

·T70 as the space-filling solute are shown to conform reasonably well with a quant. expression describing interaction between an impenetrable sphere and an ideal Brownian path (K.M. Jansons and C.G. Phillips, J. Colloid Interface Sci., 137 (1990) 75).

L17 ANSWER 7 OF 14 CAPLUS COPYRIGHT 2002 ACS
1992:23075 Document No. 116:23075 Water-based black inks and printing processes. Iwata, Kazuo; Shirota, Katsuhiro; Nishiwaki, Osamu (Canon K. K., Japan). Jpn. Kokai Tokkyo Koho JP 02233783 A2 19900917 Heisei, 8 pp. (Japanese). CODEN: JKXXAF. APPLICATION: JP 1989-52813 19890307.
GI

/ Structure 1 in file .gra /

AB The title inks giving discoloration-resistant images contain water-sol. org. solvents, water, and water-sol. dyes contg. azo compds. I (X1-X4 = H, Li, Na, K, quaternary ammonium) and/or II (X5-X7 = H, Li, Na, K, quaternary ammonium), phtyhalocyanine dyes, and metal-contg. azo dyes with red-purple-blue color tone. Printing processes using the inks are also claimed. Thus, II (X5-X7 = Li, H; Li:H = 2:1) 1.0, C.I. Direct Blue 199 1.0, C.I. Direct Violet 47 0.3, ***polyethylene*** ***glycol*** ***20*** .0, ethylene glycol 15.0, 1,3-dimethyl-2-imidazolidinone 5.0, triethanolamine 0.1, 1,2-benzisothiazolin-3-one 0.01, and water 58.0 parts were stirred, then filtered under pressure to give an ink, which when used for jet-printing gave water- and light-resistant images.

L17 ANSWER 8 OF 14 CAPLUS COPYRIGHT 2002 ACS
1991:415649 Document No. 115:15649 Wettable, flexible, oxygen-permeable contact lens containing block copolymer polysiloxane-polyoxyalkylene backbone units. Robertson, J. Richard; Su, Kai C.; Goldenberg, Merrill S.; Mueller, Karl F. (Ciba-Geigy A.-G., Switz.). Eur. Pat. Appl. EP 395583 A2 19901031, 29 pp. DESIGNATED STATES: R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE. (German). CODEN: EPXXDW. APPLICATION: EP 1990-810308 19900418. PRIORITY: US 1989-342848 19890424; US 1989-342847 19890424.
AB The title copolymers comprise the segment R9Sil(LhR9Sil)nLhR10A(LR10A)n [R9 = bond, NR1, etc.; R10 = NR1, O; R1 = H, alkyl, Ph; n = h = 0, 1; m, n = 0, 1-3; Sil = R2b(SiR3R4O)y SiR3R4R5fR9; L = L1R6L2; A = [CR72(CR82)rCR72O)tCR72(CR82)rCR72R10; R2, R5 = alkylene, CO, alkylenecarbonyl, etc.; f = 1-10; b = 0, 1; y = 1-200; R3, R4 = alkyl; L1, L2 = CO2, CONH, CO, bond; R6 = aliph. hydrocarbyl, etc.; R7 = H, halo, alkyl, (un)substituted aryl, etc.; R8 = H, alkyl, aryloxy, etc.; r = 0, 1-4; t = 3-200]. Lenses were made by UV curing of a soln. contg. dimethylsiloxane ***23*** .0, isophorone diisocyanate 4.6, ***polyethylene*** ***glycol*** ***20*** .7, isocyanotoethyl methacrylate 3.2, benzoin Me ether 0.14, and iso-PrAcO 48.45%.

L17 ANSWER 9 OF 14 CAPLUS COPYRIGHT 2002 ACS
1990:520681 Document No. 113:120681 Prolongation of release of theophylline derivatives from cellulose acetate-based tablets. Guyonnet, T.; Brossard, C.; Lefort des Ylouses, D. (UFR Pharm., Univ. Limoges, Limoges, 87025, Fr.). Journal de Pharmacie de Belgique, 45(2), 111-19 (French) 1990. CODEN: JPBEAJ. ISSN: 0047-2166.
AB Sustained-release tablets were prepd. from theophylline, dyphylline, and proxyphylline by using cellulose acetate as the matrix polymer. The drug release increased with increasing polymer content in the matrix and increasing theophylline amt. A mixed matrix comprising cellulose acetate and dibasic Ca phosphate was used for direct tablet compression. The drug release was optimized either by ***23*** factorial anal. or by multiple linear regression. The drug soly. had a great effect on the release rate. Sustained-release tablets could not be obtained when the soly. was high. With dyphylline and proxyphylline, addnl. coating of the matrix surface of tablets by using ***PEG*** ***20*** ,000 permitted the prevention of the premature erosion of tablets and a massive amt. of drug being released.

L17 ANSWER 10 OF 14 CAPLUS COPYRIGHT 2002 ACS

1985:467785 Document No. 103:67785 Evaluation of a new HDL2/HDL3 quantitation method based on precipitation with polyethylene glycol. Kostner, G. M.; Molinari, E.; Pichler, P. (Inst. Med. Biochem., Univ. Graz, Graz, A-8010, Austria). Clinica Chimica Acta, 148(2), 139-47 (English) 1985. CODEN: CCATAR. ISSN: 0009-8981.

AB A method for detn. of high-d. lipoprotein (HDL) 2 and 3 in human serum or plasma samples is described which is based on pptn. with polyethylene glycol (PEG) using the Quintolip test kit. The test kit consists of the following 2 solns.: soln. A (95% ***PEG*** ***20*** ,000 in 0.1M Na phosphate buffer, pH 6.5) for pptn. of very-low-d. and low-d. lipoproteins (LDL); and soln. B (15% ***PEG*** ***20*** ,000 in 0.1M Na phosphate buffer, pH 7.5) for pptn. of LDL and HDL2, leaving only HDL3 in the supernatant. The cholesterol content of HDL was detd. enzymically, and HDL2 cholesterol was calcd. from total HDL cholesterol minus HDL3 cholesterol. The PEG method compared favorably with other methods and had within-assay and day-to-day relative std. deviations of 0.35-0.80 and 1.8-2.2%, resp., for HDL cholesterol and 0.57-1. ***23*** and 2.5-2.8%, resp., for HDL2 cholesterol. The method is well suited for clin. anal. due to its simplicity, accuracy, and specificity.

L17 ANSWER 11 OF 14 CAPLUS COPYRIGHT 2002 ACS

1982:158182 Document No. 96:158182 Crystallizations and preliminary x-ray studies of calotropins DI and DII. Pal, Gour P.; Sinha, Nirmal K.; Saenger, Wolfram (Abt. Chem., Max-Planck-Inst. Exp. Med., Goettingen, D-3400, Fed. Rep. Ger.). J. Mol. Biol., 153(4), 1157-9 (English) 1981. CODEN: JMOBAK. ISSN: 0022-2836.

AB Crystals of calotropin DI (mol. wt. ***23*** ,400) were prepd. by microdialysis against 5% (wt./vol.) ***polyethylene*** ***glycol*** ***20*** ,000 in water, pH 7.0. They had orthorhombic space group P212121 with cell parameters a = 57.5, b = 86.2, c = 40.3 .ANG.. Crystals of calotropin DII (mol. wt. 24,000), prepd. by the same technique, displayed monoclinic space group C2 with cell parameters a = 135.8, b = 32.0, c = 47.7 .ANG., .beta. = 103.80.degree.. In both cases, there was only one mol. in the asym. unit.

L17 ANSWER 12 OF 14 CAPLUS COPYRIGHT 2002 ACS

1981:546162 Document No. 95:146162 Dried membrane with immobilized enzyme. (Tokyo Shibaura Electric Co., Ltd., Japan). Jpn. Kokai Tokkyo Koho JP 56064789 19810602 Showa, 5 pp. (Japanese). CODEN: JKXXAF. APPLICATION: JP 1979-140491 19791101.

AB A membrane with an immobilized enzyme contg. .gtoreq.1 of the following compds.: nonionic surfactant, ethylene glycol, polyethylene glycol, glycerol, BuOH, sorbitol, and mannitol, is prepd. by soaking the immobilized enzyme-membrane in a soln. contg. .gtoreq.1 of the above compds. The immobilized enzyme-membrane thus treated may be dried for storage or shipment and is readily restored to its original state by moistening with water. The immobilized enzyme(s) remains stable throughout the drying, storage, and remoistening. Thus, a porous cellulose triacetate membrane in which ***uricase*** was immobilized was soaked in a soln. contg. ***polyethylene*** ***glycol*** (***10*** %), glycerol (50%), and H2O (40%) and lyophilized to obtain a dried immobilized ***uricase*** -membrane. The ***uricase*** -membrane prepn. is stable during storage and is restored to its original state by rinsing with water.

L17 ANSWER 13 OF 14 CAPLUS COPYRIGHT 2002 ACS

1972:37741 Document No. 76:37741 Donnan equilibrium of sodium bromide in poly(methacrylic acid) solutions in aqueous formamide. Casorati, Ernesto (Ist. Chim. Anal., Univ. Torino, Turin, Italy). Ann. Chim. (Rome), 61(7-8), 457-73 (Italian) 1971. CODEN: ANCRAI.

AB The effect of the degree of neutralization (.alpha.) of poly(methacrylic acid) (I) (mol. wt. .apprx.3.times.105, calcd. from the intrinsic viscosity, [.eta.]=1. ***23*** dl/g, of its Na salt), of the molarity mm of Na polymethacrylate, and of the molarity ms of NaBr on the Donnan equil. (Strauss et al., 1958 and Vink, 1963) was studied by measuring the ratio of the activity coeffs. of NaBr in formamide contg. partially neutralized I in formamide contg. 0.54% water and polyethylene glycol (***PEG*** ***20000***), resp. This was done in concn. osmometers (Alexandrowicz, 1959), placing the NaBr soln. in formamide on one side of the membrane and NaBr in the polyelectrolyte on the other, and following the transfer of NaBr by argentometry. Establishment of salt and osmotic

equil. was probed by placing PEG 15000 solns. (0-1.5%) on the polyelectrolyte side and measuring level changes. Salt equil. was reached in a few hr but osmotic equil. required considerably longer. Activity coeffs. dropped from 1.0 to 0.7 when .alpha. increased from 0 to 0.8 (const. ms and ma), from 1.0 to 0.75-0.85 (depending on .alpha.) when mm increased from 0 to 0.068, and increased from 0 to 0.75 when ms increased from 0 to 0.08; they also decreased linearly without increasing .alpha..mm (20.+-.1.degree.). The effective "thermodynamic degree of ionization" .mu.=2 (m1s-ms)/.alpha..mm (in which m1s and ms are NaBr molarities on both sides of the membrane) dropped from 0.7 to 0.2 when .alpha. increased from 0 to 0.8, and increased slowly with increasing values of Ms. Values of .mu. were related to the practical osmotic coeff. of the pure electrolyte by applying the empirical additivity rule.

L17 ANSWER 14 OF 14 CAPLUS COPYRIGHT 2002 ACS
1968:477026 Document No. 69:77026 Condensed 2-azetidinones. II. Isomeric 3-phenyl-1-azabicyclo[4,2,0]octan-2-ones. Moll, F. (Univ. Tuebingen, Tuebingen, Ger.). Arch. Pharm. (Weinheim), 301(4), 250-62 (German) 1968. CODEN: APBDAJ.

AB .alpha.-Phenyl-.alpha.-pyrid-2-ylacetonitrile was converted into the corresponding amide, and reduced to .alpha.-phenyl-.alpha.-piperid-2-ylacetamide, which was treated with 18% HCl 6 hrs. at 110.degree. to give .alpha.-phenyl-.alpha.-piperid-2-ylacetic acid-HCl (I). Attempts to remove the HCl from I gave mainly piperidylacetic acid. .alpha.-Ethyl-.alpha.-phenyl-.alpha.-piperid-2-ylacetamide was similarly obtained, but could not be converted into .alpha.-ethyl-.alpha.-phenyl-.alpha.-piperid-2-ylacetic acid-HCl. .alpha.-Phenyl-.alpha.-piperid-2-ylacetyl chloride-HCl (II) was prepd. from .alpha.-phenyl-.alpha.-piperid-2-ylacetic acid and SOCl2. II was treated with Et3N 24 hrs. at room temp. to give 3-phenyl-1-azabicyclo[4.2.0]octan-2-one (III), also obtained by treating I with dicyclohexylcarbodiimide. The isomers of II were sepd. by gas chromatog. on ***polyethylene*** ***glycol*** (***20*** ,000) at 220.degree., 106 ml./min. He. The cis isomer, m. 70.degree., had a retention time of 20 min. and the trans isomer ***23*** min. III was also prepd. by photolysis of phenylglyoxylpiperidine dianzo ketone as described by E. J. Corey and A. M. Felix (1965). The trans isomer was the major product in this reaction.

=> E ENSOR C/AU

=> S E3-E5 AND E8-E10
3 "ENSOR C"/AU
2 "ENSOR C M"/AU
10 "ENSOR C MARK"/AU
1 "ENSOR CHARLERS MARK"/AU
12 "ENSOR CHARLES"/AU
20 "ENSOR CHARLES MARK"/AU
L18 0 ("ENSOR C"/AU OR "ENSOR C M"/AU OR "ENSOR C MARK"/AU) AND ("ENSOR CHARLERS MARK"/AU OR "ENSOR CHARLES"/AU OR "ENSOR CHARLES MARK"/AU)

=> S E3-E5,E8-E10
3 "ENSOR C"/AU
2 "ENSOR C M"/AU
10 "ENSOR C MARK"/AU
1 "ENSOR CHARLERS MARK"/AU
12 "ENSOR CHARLES"/AU
20 "ENSOR CHARLES MARK"/AU
L19 48 ("ENSOR C"/AU OR "ENSOR C M"/AU OR "ENSOR C MARK"/AU OR "ENSOR CHARLERS MARK"/AU OR "ENSOR CHARLES"/AU OR "ENSOR CHARLES MARK"/AU)

=> E CLARK M/AU
=> S E3,E4,E83-E85
110 "CLARK M"/AU
53 "CLARK M A"/AU
10 "CLARK MARK"/AU
2 "CLARK MARK A"/AU
1 "CLARK MARK ALAN"/AU
L20 176 ("CLARK M"/AU OR "CLARK M A"/AU OR "CLARK MARK"/AU OR "CLARK

MARK A"/AU OR "CLARK MARK ALAN"/AU)

=> E HOLTSBERG/AU
=> S E4-E9
1 "HOLTSBERG F W"/AU
1 "HOLTSBERG FREDERIC W"/AU
3 "HOLTSBERG FREDERICK"/AU
12 "HOLTSBERG FREDERICK W"/AU
3 "HOLTSBERG FREDERICK WAYNE"/AU
1 "HOLTSBERG FREDRICK W"/AU
L21 21 ("HOLTSBERG F W"/AU OR "HOLTSBERG FREDERIC W"/AU OR "HOLTSBERG FREDERICK"/AU OR "HOLTSBERG FREDERICK W"/AU OR "HOLTSBERG FREDERICK WAYNE"/AU OR "HOLTSBERG FREDRICK W"/AU)

=> S L19,L20,L21
L22 239 (L19 OR L20 OR L21)

=> S L22 AND L2
L23 1 L22 AND L2

=> S L22 AND L8
L24 5 L22 AND L8

=> S L23,L24
L25 5 (L23 OR L24)

=> S L10 AND L2
L26 2 L10 AND L2

=> S L26,L13
L27 4 (L26 OR L13)

=> S L27,L25
L28 8 (L27 OR L25)

=> D 1-8 CBIB ABS

L28 ANSWER 1 OF 8 CAPLUS COPYRIGHT 2002 ACS
2002:779615 Pegylated arginine deiminase (ADI-SS PEG20,000 mw) inhibits human melanomas and hepatocellular carcinomas in vitro and in vivo. ***Ensor,*** *** Charles Mark*** ; ***Holtsberg, Frederick W.*** ; Bomalaski, John S.; Clark, Mike A. (Department of Biology, Advanced Science and Technology Commercialization Center, Phoenix Pharmacologics, Inc., University of Kentucky, Lexington, KY, 40506, USA). Cancer Research, 62(19), 5443-5450 (English) 2002. CODEN: CNREA8. ISSN: 0008-5472. Publisher: American Association for Cancer Research.

AB Some murine melanomas and hepatocellular carcinomas (HCCs) have been shown to be auxotrophic for arginine. Arginine deiminase (ADI; EC 3.5.3.6.), an arginine-degrading enzyme isolated from Mycoplasma, can inhibit growth of these tumors. We found that ADI was specific for arginine and did not degrade other amino acids. Although arginine is not an essential amino acid for most cells, all human melanomas and HCCs tested were found to be inhibited by ADI in vitro. Arginine is synthesized from citrulline in two steps by argininosuccinate synthetase and argininosuccinate lyase. Melanomas and HCCs did not express argininosuccinate synthetase mRNA but did express argininosuccinate lyase mRNA, suggesting that the arginine auxotrophy of these cells was a result of an inability to produce argininosuccinate synthetase. Human melanomas and HCCs were transfected with an expression plasmid contg. argininosuccinate synthetase cDNA. The transfected cells were much more resistant to ADI than the parental cells in vitro and in vivo. Initial attempts to use ADI in vivo indicated that this enzyme had little efficacy, consistent with its short circulation half-life. Formulation of ADI with ***polyethylene*** ***glycol*** to produce ADI-SS PEG20,000 mw resulted in an enzyme with a much longer circulation half-life that, and although equally effective in vitro, was more efficacious in the treatment of mice implanted with human melanomas and HCCs. These data indicate that sensitivity of melanoma and HCC is due to the absence of argininosuccinate synthetase in these cells and that an effective formulation of ADI, which causes a sustained decrease in arginine, may be a useful treatment for arginine auxotrophic tumors including melanoma and HCC.

L28 ANSWER 2 OF 8 CAPLUS COPYRIGHT 2002 ACS

2002:762731 ***Uricase*** formulated with ***polyethylene*** ***glycol*** (***uricase*** - ***PEG*** ***20***): biochemical rationale and preclinical studies. Bomalaski, John S.; ***Holtsberg,*** *** Frederick W.*** ; ***Ensor, C. Mark*** ; Clark, Mike A. (Department of Biology, University of Kentucky, Lexington, KY, USA). Journal of Rheumatology, 29(9), 1942-1949 (English) 2002. CODEN: JRHUA9. ISSN: 0315-162X. Publisher: Journal of Rheumatology Publishing Co. Ltd..

AB Objective. Humans have a non-sense codon inserted into the 5 prime end of the open reading frame of urate oxidase, and thus express an enzymically inactive fragment of this enzyme; and consequently are unable to metabolize uric acid into allantoin and are prone to develop hyperuricemia and gout. Various urate oxidases (***uricase***) from mammals and microorganisms have been administered to humans with hyperuricemia and gout. Although successful in lowering plasma uric acid, these therapies have had limited application due to undesirable biochem. properties of the enzymes used, the short circulating half-life, and inherent antigenicity of these prepns. We compared urate oxidase from a variety of sources for specific enzyme activity, pH optimum, affinity, and retention of enzyme activity under physiol. conditions. A variety of ***polyethylene*** ***glycols*** (***PEG***) were tested to formulate ***uricase*** . Urate oxidase from Candida utilis had more favorable enzymic properties and ***PEG*** of 20,000 MW (termed ***uricase*** - ***PEG*** ***20***) had greatly reduced antigenicity and increased circulating half-life as compared to those previously described. Conclusion. It is anticipated that ***uricase*** - ***PEG*** ***20*** may have utility as a treatment for hyperuricemia and gout.

L28 ANSWER 3 OF 8 CAPLUS COPYRIGHT 2002 ACS

2002:393503 Enzymic degradation of plasma arginine using arginine deiminase inhibits nitric oxide production and protects mice from the lethal effects of tumour necrosis factor .alpha. and endotoxin. Thomas, J. Brandon; ***Holtsberg, Frederick W.*** ; ***Ensor, C. Mark*** ; Bomalaski, John S.; Clark, Mike A. (Department of Biology, University of Kentucky, Lexington, KY, 40506, USA). Biochemical Journal, 363(3), 581-587 (English) 2002. CODEN: BIJOAK. ISSN: 0264-6021. Publisher: Portland Press Ltd..

AB Septic shock is mediated in part by nitric oxide (NO) and tumor necrosis factor .alpha. (TNF.alpha.). NO is synthesized primarily from extracellular arginine. We tested the ability of an arginine-degrading enzyme to inhibit NO prodn. in mice and to protect mice from the hypotension and lethality that occur after the administration of TNF.alpha. or endotoxin. Treatment of BALB/c mice with arginine deiminase (ADI) formulated with succinimidyl succinimide ***polyethylene*** ***glycol*** of Mr 20000 (ADI-SS PEG20000) eliminated all measurable plasma arginine (from normal levels of .apprx. 155 .mu.M arginine to 2 .mu.M). In addn., ADI-SS PEG20000 also inhibited the prodn. of NO, as quantified by plasma nitrate + nitrite. Treatment of mice with TNF.alpha. or endotoxin resulted in a dose-dependent increase in NO prodn. and lethality. Pre-treatment of mice with ADI-SS PEG20000 resulted in increased resistance to the lethal effects of TNF.alpha. and endotoxin. These observations are consistent with NO prodn. resulting, to some extent, from the metab. of extracellular arginine. The toxic effects of TNF.alpha. and endotoxin may be partially inhibited by enzymic degrdn. of plasma arginine by ADI-SS PEG20000. Interestingly, pretreatment with ADI-SS PEG20000 did not inhibit the antitumor activity of TNF.alpha. in vitro or in vivo. This treatment may allow greater amts. of TNF.alpha., as well as other cytokines, to be administered while abrogating side effects such as hypotension and death.

L28 ANSWER 4 OF 8 CAPLUS COPYRIGHT 2002 ACS

2002:258834 Poly(ethylene glycol) (***PEG***) conjugated arginine deiminase: effects of ***PEG*** formulations on its pharmacological properties. ***Holtsberg, Frederick W.*** ; ***Ensor, Charles*** *** Mark*** ; Steiner, Marion R.; Bomalaski, John S.; Clark, Mike A. (Department of Biology, University of Kentucky, Lexington, KY, 40506, USA). Journal of Controlled Release, 80(1-3), 259-271 (English) 2002. CODEN: JCREEC. ISSN: 0168-3659. Publisher: Elsevier Science Ltd..

AB Some tumors, such as melanomas and hepatocellular carcinomas, have a unique nutritional requirement for arginine. Thus, enzymic degrdn. of

extracellular arginine is one possible means for inhibiting these tumors. Arginine deiminase is an arginine degrading enzyme (ADI) that has been studied as an anti-cancer enzyme. However, ADI has a short serum half-life and, as a microbial enzyme, is highly immunogenic. Formulation of other therapeutic proteins with poly(ethylene glycol) (***PEG***) has overcome these problems. Here, ADI- ***PEGs*** were synthesized using ***PEGs*** of varying size, structure (linear or branched chain) and linker chemistries. All ADI- ***PEGs*** retained .apprx.50% of enzyme activity when ***PEG*** was covalently attached to .apprx.40% of the primary amines irresp. of the ***PEG*** mol. wt. or attachment chem. used. However, it was obsd. that, as the ***PEG*** size increases to 20 kDa, there was a corresponding increase in the pharmacokinetic (pK) and pharmacodynamic (pD) properties of the formulation. Variation in ***PEG*** linker or structure, or the use of ***PEGs*** >20,000 mw, did not affect the pK or pD. As has been shown with other therapeutic proteins, repeated injection of ADI- ***PEG*** into exptl. animals resulted in significantly lower titers of antibodies against this protein than unmodified ADI. These data suggest that formulation of ADI with ***PEG*** of 20,000 mw results is the optimal method for formulating this promising therapeutic agent.

L28 ANSWER 5 OF 8 CAPLUS COPYRIGHT 2002 ACS

2001:816931 Document No. 135:354694 Mutated form of arginine deiminase from Mycoplasma hominis and uses in therapy. ***Ensor, Charles Mark*** ; ***Holtsberg, Frederick Wayne*** ; Clark, Mike A. (Phoenix Pharmacologics, Inc., USA). PCT Int. Appl. WO 2001083774 A2 20011108, 34 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-US14116 20010502. PRIORITY: US 2000-564559 20000504.

AB The present invention discloses arginine deiminase that is genetically modified for more efficient manufg. and processing. The modified arginine deiminase contains glutamic acid at position of 112 and serine at position 210, which showed a higher yield and shorter time and less diln. required for renaturation compared to wild-type protein. The present invention discloses recombinant DNA mols. and vectors and other therapeutic and pharmaceutical compns. The invention demonstrated that formulation of arginine deiminase with ***polyethylene*** ***glycol*** , i.e. PEGylation, can reduce the antigenicity of the protein and greatly increase its circulating half-life. The present invention also discloses methods for prepg. modified arginine deiminase as well as methods of treating cancer and other disease states using modified arginine deiminase.

L28 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2002 ACS

2001:417471 Document No. 135:142105 Immunological Properties of ***Uricase*** Conjugated to Neutral Soluble Polymers. Caliceti, Paolo; Schiavon, Oddone; Veronese, Francesco M. (Department of Pharmaceutical Sciences, University of Padua, Padua, Italy). Bioconjugate Chemistry, 12(4), 515-522 (English) 2001. CODEN: BCCHES. ISSN: 1043-1802. Publisher: American Chemical Society.

AB For a comparative study of immunol. properties of protein-polymer conjugates, ***uricase*** was modified with poly(N-vinylpyrrolidone) 6000, poly(N-acryloylmorpholine) 6000, (c) branched monomethoxy ***polyethylene*** ***glycol*** ***10*** ,000, and (d) linear monomethoxy polyethylene glycol 5000 Da. Spectroscopic studies performed by UV, fluorescence, and CD did not show any relevant difference in protein conformation among the native and the conjugates. Immunol. studies showed that both ***uricase*** antigenicity and immunogenicity were altered by polymer conjugation to an extent that depended upon the polymer compn.; in particular, monomethoxypolyethylene glycol 10,000 Da remarkably reduced the protein antigenicity, while unexpectedly, the poly(N-vinylpyrrolidone) deriv. presented higher antigenicity than the native protein. In Balb/c mice, the native protein elicited a rapid and intense immunoresponse whereas all the conjugates induced a lower prodn. of anti-native ***uricase*** antibodies. The rank order of

immunogenicity was native ***uricase*** > ***uricase*** -poly(N-vinylpyrrolidone) .gtoreq. ***uricase*** -poly(N-acryloylmorpholine) > ***uricase*** -monomethoxy polyethylene glycol 5000 Da > ***uricase*** -monomethoxy ***polyethylene*** ***glycol*** ***10000*** Da. The 4 conjugates also induced anti-polymer immunoresponse. Anti poly(N-vinylpyrrolidone) and anti poly(N-acryloylmorpholine) antibodies were generated from the first immunization, while low levels of anti-polymer antibodies were found with both polyethylene glycol conjugates only after the second immunization.

L28 ANSWER 7 OF 8 CAPLUS COPYRIGHT 2002 ACS
1997:632602 Document No. 127:283170 Agent and process for oxidative dyeing of keratin fibers. Kunz, Manuela; Le Cruer, Dominique (Wella Aktiengesellschaft, Germany). Eur. Pat. Appl. EP 795313 A2 19970917, 11 pp. DESIGNATED STATES: R: DE, ES, FR, GB, IT. (German). CODEN: EPXXDW. APPLICATION: EP 1996-119343 19961203. PRIORITY: DE 1996-19610392 19960316.
GI

/ Structure 2 in file .gra /

AB An oxidative hair dye compn. comprises an O2 oxidoreductase/substrate system, a peroxidase, and a m-phenylenediamine coupler [I; C1-6 alkoxy, (substituted) C1-6 alkyl; R2, R3 = H, (substituted) C1-6 alkyl or mono- or dioxaalkyl; R4 = H, C1-6 alkyl] and has a pH of 6-9.5. Such compns.do not damage the hair and provide intense coloration, esp. when combined with direct dyes. Thus, a hair dye compn. contg. hydroxyethyl-p-phenylenediamine sulfate 0.025 mol, 2-amino-4-(2'-hydroxyethyl)aminoanisole sulfate 0.025 mol, glucose oxidase (EC 1.1.3.4) 400 U, peroxidase (EC 1.11.1.7) 400 U, iso-PrOH 5.000,, 1,2-propanediol 2.000, ***PEG*** - ***20*** stearyl ether 1.400, glycerin 1.000, glucose 1.000, di-Na EDTA 0.300, ascorbic acid 0.100, 2-amino-6-chloro-4-nitrophenol 0.075, and 0.1M borate buffer to 100.000 g, adjusted to pH 7.7 and applied to bleached hair for 30 or 60 min at room temp., conferred an intense brown color on the hair.

L28 ANSWER 8 OF 8 CAPLUS COPYRIGHT 2002 ACS
1981:546162 Document No. 95:146162 Dried membrane with immobilized enzyme. (Tokyo Shibaura Electric Co., Ltd., Japan). Jpn. Kokai Tokkyo Koho JP 56064789 19810602 Showa, 5 pp. (Japanese). CODEN: JKXXAF. APPLICATION: JP 1979-140491 19791101.
AB A membrane with an immobilized enzyme contg. .gtoreq.1 of the following compds.: nonionic surfactant, ethylene glycol, polyethylene glycol, glycerol, BuOH, sorbitol, and mannitol, is prepd. by soaking the immobilized enzyme-membrane in a soln. contg. .gtoreq.1 of the above compds. The immobilized enzyme-membrane thus treated may be dried for storage or shipment and is readily restored to its original state by moistening with water. The immobilized enzyme(s) remains stable throughout the drying, storage, and remoistening. Thus, a porous cellulose triacetate membrane in which ***uricase*** was immobilized was soaked in a soln. contg. ***polyethylene*** ***glycol*** (***10*** %), glycerol (50%), and H2O (40%) and lyophilized to obtain a dried immobilized ***uricase*** -membrane. The ***uricase*** -membrane prepn. is stable during storage and is restored to its original state by rinsing with water.

Title: US-09-921-380-6

RESULT 1
AAR43067
ID AAR43067 standard; Protein; 303 AA.
XX
AC AAR43067;
XX
DT 25-MAY-1994 (first entry)
XX
DE Uricase enzyme.
XX
KW Uricase; Candida utilis; detection; uric acid.
XX
OS Candida utilis.
XX
PN DE4316505-A.
XX
PD 18-NOV-1993.
XX
PF 17-MAY-1993; 93DE-4316505.
XX
PR 15-MAY-1992; 92JP-0123898.
XX
PA (KIKK) KIKKOMAN CORP.
XX
PI Ichikawa T, Koyama Y, Nakano E;
XX
DR WPI; 1993-370056/47.
DR N-PSDB; AAQ50608.
XX
PT DNA coding for Candida utilis uricase enzyme - for prodn. of
PT recombinant uricase used for quantitative determn. of uric acid
PT in blood or urine
XX
PS Claim 9; Page 6-7; 8pp; German.
XX
CC Uricase is useful as a reagent for quantitive determination of uric
CC acid in blood or urine. E. coli transformed with the Candida utilis
CC uricase gene are capable of producing uricase when cultured in media
CC not containing uric acid.
XX
SQ Sequence 303 AA;

Query Match 99.7%; Score 1587; DB 14; Length 303;
Best Local Similarity 99.7%; Pred. No. 1.3e-139;
Matches 302; Conservative 1; Mismatches 0; Indels 0; Gaps 0;

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Qy     301 TKL 303
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Db     301 TKL 303
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RESULT 1
US-08-701-952A-1
; Sequence 1, Application US/08701952A
; Patent No. 5700674
; GENERAL INFORMATION:
; APPLICANT: Koyama et al., Yasuji
; TITLE OF INVENTION: MUTANT URICASE, A MUTANT URICASE GENE, A
; TITLE OF INVENTION: NOVEL RECOMBINANT DNA, AND A PROCESS FOR PRODUCING MUTANT
; TITLE OF INVENTION: URICASE
; NUMBER OF SEQUENCES: 4
; CORRESPONDENCE ADDRESS:
; ADDRESSEE: Fish & Richardson P.C.
; STREET: 601 Thirteenth Street, NW
; CITY: Washington
; STATE: DC
; COUNTRY: USA
; ZIP: 20005
; COMPUTER READABLE FORM:
; MEDIUM TYPE: Floppy disk
; COMPUTER: IBM PC compatible
; OPERATING SYSTEM: PC-DOS/MS-DOS
; SOFTWARE: PatentIn Release #1.0, Version #1.30
; CURRENT APPLICATION DATA:
; APPLICATION NUMBER: US/08/701,952A
; FILING DATE: 23-AUG-1996
; CLASSIFICATION: 435
; PRIOR APPLICATION DATA:
; APPLICATION NUMBER: JP 216239/1995
; FILING DATE: 24-AUG-1995
; ATTORNEY/AGENT INFORMATION:
; NAME: Ellison, Eldora L.
; REGISTRATION NUMBER: 39,967
; REFERENCE/DOCKET NUMBER: 08206/003001
; TELECOMMUNICATION INFORMATION:
; TELEPHONE: 202/783-5070
; TELEFAX: 202/783-2331
; INFORMATION FOR SEQ ID NO: 1:
; SEQUENCE CHARACTERISTICS:
; LENGTH: 303 amino acids
; TYPE: amino acid
; STRANDEDNESS: not relevant
; TOPOLOGY: linear
; MOLECULE TYPE: protein
US-08-701-952A-1

Query Match 99.7%; Score 1587; DB 1; Length 303;
Best Local Similarity 99.7%; Pred. No. 1.7e-146;
Matches 302; Conservative 1; Mismatches 0; Indels 0; Gaps 0;

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Qy     301 TKL 303
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Db     301 TKL 303


RESULT 2
US-08-938-471-1
; Sequence 1, Application US/08938471
; Patent No. 5801036
;  GENERAL INFORMATION:
;    APPLICANT:  Koyama et al., Yasuji
;    TITLE OF INVENTION:  MUTANT URICASE, A MUTANT URICASE GENE, A
;    TITLE OF INVENTION:  NOVEL RECOMBINANT DNA, AND A PROCESS FOR PRODUCING MUTANT
;    TITLE OF INVENTION:  URICASE
;    NUMBER OF SEQUENCES:  4
;    CORRESPONDENCE ADDRESS:
;      ADDRESSEE:  Fish & Richardson P.C.
;      STREET:  601 Thirteenth Street, NW
;      CITY:  Washington
;      STATE:  DC
;      COUNTRY:  USA
;      ZIP:  20005
;    COMPUTER READABLE FORM:
;      MEDIUM TYPE:  Floppy disk
;      COMPUTER:  IBM PC compatible
;      OPERATING SYSTEM:  PC-DOS/MS-DOS
;      SOFTWARE:  PatentIn Release #1.0, Version #1.30
;    CURRENT APPLICATION DATA:
;      APPLICATION NUMBER:  US/08/938,471
;      FILING DATE:
;      CLASSIFICATION:  435
;    PRIOR APPLICATION DATA:
;      APPLICATION NUMBER:  US 08/701,952
;      FILING DATE:  23-AUG-1996
;      APPLICATION NUMBER:  JP 216239/1995
;      FILING DATE:  24-AUG-1995
;    ATTORNEY/AGENT INFORMATION:
;      NAME:  Ellison, Eldora L.
;      REGISTRATION NUMBER:  39,967
;      REFERENCE/DOCKET NUMBER:  08206/003001
;    TELECOMMUNICATION INFORMATION:
;      TELEPHONE:  202/783-5070
;      TELEFAX:  202/783-2331
;  INFORMATION FOR SEQ ID NO:  1:
;    SEQUENCE CHARACTERISTICS:
;      LENGTH:  303 amino acids
;      TYPE:  amino acid
;      STRANDEDNESS:  not relevant
;      TOPOLOGY:  linear
;    MOLECULE TYPE:  protein
US-08-938-471-1

  Query Match             99.7%;  Score 1587;  DB 1;  Length 303;
  Best Local Similarity   99.7%;  Pred. No. 1.7e-146;
  Matches  302;  Conservative    1;  Mismatches    0;  Indels    0;  Gaps    0;

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Db     121 HSFIHEGGEKRITDLYYKRSGDYKLSSAIKDLTVLKSTGSMFYGYNKCDFTTLQPTTDRI 180

Qy     181 LSTDVDATWVWDNKKIGTVYDIAKAADKGIFDNVYNQAREITLTTFALENSPSVQATMFN 240
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Db    241 MATQILEKACSVYSVSYALPNKHYFLIDLKWKGLENDNELFYPSPHPNGLIKCTVVRKEK 300

Qy    301 TKL 303
          |||
Db    301 TKL 303


RESULT 3
US-09-921-380-5
; Sequence 5, Application US/09921380
; GENERAL INFORMATION:
;  APPLICANT: Ensor, Mark
;  APPLICANT:  Holtsberg, Frederick Wayne
;  APPLICANT:  Clark, Mike
;  TITLE OF INVENTION: PEG-Modified Uricase
;  FILE REFERENCE: PHOE0061
;  CURRENT APPLICATION NUMBER: US/09/921,380
;  CURRENT FILING DATE:  2001-08-02
;  NUMBER OF SEQ ID NOS: 6
;  SOFTWARE: PatentIn version 3.1
; SEQ ID NO 5
;   LENGTH: 303
;   TYPE: PRT
;   ORGANISM: Candida utilis
US-09-921-380-5

  Query Match           100.0%;  Score 1591;  DB 23;  Length 303;
  Best Local Similarity  100.0%;  Pred. No. 3.5e-158;
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Qy      1 MSTTLSSSTYGKDNVKFLKVKKDPQNPKKQEVMEATVTCLLEGGFDTSYTEADNSSIVPT 60
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      1 MSTTLSSSTYGKDNVKFLKVKKDPQNPKKQEVMEATVTCLLEGGFDTSYTEADNSSIVPT 60

Qy     61 DTVKNTILVLAKTTEIWPIERFAAKLATHFVEKYSHVSGVSVKIVQDRWVKYAVDGKPHD 120
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     61 DTVKNTILVLAKTTEIWPIERFAAKLATHFVEKYSHVSGVSVKIVQDRWVKYAVDGKPHD 120

Qy    121 HSFIHEGGEKRITDLYYKRSGDYKLSSAIKDLTVLKSTGSMFYGYNKCDFTTLQPTTDRI 180
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    121 HSFIHEGGEKRITDLYYKRSGDYKLSSAIKDLTVLKSTGSMFYGYNKCDFTTLQPTTDRI 180

Qy    181 LSTDVDATWVWDNKKIGTVYDIAKAADKGIFDNVYNQAREITLTTFALENSPSVQATMFN 240
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    181 LSTDVDATWVWDNKKIGTVYDIAKAADKGIFDNVYNQAREITLTTFALENSPSVQATMFN 240

Qy    241 MATQILEKACSVYSVSYALPNKHYFLIDLKWKGLENDNELFYPSPHPNGLIKCTVVRKEK 300
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    241 MATQILEKACSVYSVSYALPNKHYFLIDLKWKGLENDNELFYPSPHPNGLIKCTVVRKEK 300

Qy    301 TKL 303
          |||
Db    301 TKL 303


RESULT 4
US-09-921-380-6
; Sequence 6, Application US/09921380
; GENERAL INFORMATION:
;  APPLICANT: Ensor, Mark
;  APPLICANT:  Holtsberg, Frederick Wayne
;  APPLICANT:  Clark, Mike
;  TITLE OF INVENTION: PEG-Modified Uricase
;  FILE REFERENCE: PHOE0061
;  CURRENT APPLICATION NUMBER: US/09/921,380
;  CURRENT FILING DATE:  2001-08-02
;  NUMBER OF SEQ ID NOS: 6
;  SOFTWARE: PatentIn version 3.1
; SEQ ID NO 6
```

; LENGTH: 303
; TYPE: PRT
; ORGANISM: Candida utilis
US-09-921-380-6

  Query Match 100.0%; Score 1591; DB 23; Length 303;
  Best Local Similarity 100.0%; Pred. No. 3.5e-158;
  Matches 303; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

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Qy       1 MSTTLSSSTYGKDNVKFLKVKKDPQNPKKQEVMEATVTCLLEGGFDTSYTEADNSSIVPT 60
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1 MSTTLSSSTYGKDNVKFLKVKKDPQNPKKQEVMEATVTCLLEGGFDTSYTEADNSSIVPT 60

Qy      61 DTVKNTILVLAKTTEIWPIERFAAKLATHFVEKYSHVSGVSVKIVQDRWVKYAVDGKPHD 120
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      61 DTVKNTILVLAKTTEIWPIERFAAKLATHFVEKYSHVSGVSVKIVQDRWVKYAVDGKPHD 120

Qy     121 HSFIHEGGEKRITDLYYKRSGDYKLSSAIKDLTVLKSTGSMFYGYNKCDFTTLQPTTDRI 180
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     121 HSFIHEGGEKRITDLYYKRSGDYKLSSAIKDLTVLKSTGSMFYGYNKCDFTTLQPTTDRI 180

Qy     181 LSTDVDATWVWDNKKIGTVYDIAKAADKGIFDNVYNQAREITLTTFALENSPSVQATMFN 240
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     181 LSTDVDATWVWDNKKIGTVYDIAKAADKGIFDNVYNQAREITLTTFALENSPSVQATMFN 240

Qy     241 MATQILEKACSVYSVSYALPNKHYFLIDLKWKGLENDNELFYPSPHPNGLIKCTVVRKEK 300
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     241 MATQILEKACSVYSVSYALPNKHYFLIDLKWKGLENDNELFYPSPHPNGLIKCTVVRKEK 300

Qy     301 TKL 303
          |||
Db     301 TKL 303
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RESULT 5
US-08-062-963-2
; Sequence 2, Application US/08062963
; GENERAL INFORMATION:
;   APPLICANT: Koyama, Yasuji
;   APPLICANT: Ichikawa, Toshio
;   APPLICANT: Nakano, Eiichi
;   TITLE OF INVENTION: A URICASE GENE, A RECOMBINANT DNA, AND A
;   TITLE OF INVENTION: PROCESS FOR THE PRODUCTION OF URICASE
;   NUMBER OF SEQUENCES: 5
;   CORRESPONDENCE ADDRESS:
;   ADDRESSEE: Limbach & Limbach
;   STREET: 2001 Ferry Building
;   CITY: San Francisco
;   STATE: CA
;   COUNTRY: USA
;   ZIP: 94111
;   COMPUTER READABLE FORM:
;   MEDIUM TYPE: Floppy disk
;   COMPUTER: IBM PC compatible
;   OPERATING SYSTEM: PC-DOS/MS-DOS
;   SOFTWARE: PatentIn Release #1.0, Version #1.25
;   CURRENT APPLICATION DATA:
;   APPLICATION NUMBER: US/08/062,963
;   FILING DATE: 19930514
;   CLASSIFICATION: 435
;   ATTORNEY/AGENT INFORMATION:
;   NAME: Dergosits, Michael E.
;   REGISTRATION NUMBER: 31,243
;   REFERENCE/DOCKET NUMBER: HIRA-01100
;   TELECOMMUNICATION INFORMATION:
;   TELEPHONE: 415-433-4150
;   TELEFAX: 415-433-8716
; INFORMATION FOR SEQ ID NO: 2:
;   SEQUENCE CHARACTERISTICS:
;   LENGTH: 303 amino acids
;   TYPE: amino acid

; TOPOLOGY: linear
; MOLECULE TYPE: protein
; HYPOTHETICAL: NO
; ANTI-SENSE: NO
; ORIGINAL SOURCE:
; ORGANISM: Candida utilis
; STRAIN: ATCC 9950
US-08-062-963-2

Query Match 99.7%; Score 1587; DB 4; Length 303;
Best Local Similarity 99.7%; Pred. No. 9.2e-158;
Matches 302; Conservative 1; Mismatches 0; Indels 0; Gaps 0;

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Qy       1 MSTTLSSSTYGKDNVKFLKVKKDPQNPKKQEVMEATVTCLLEGGFDTSYTEADNSSIVPT 60
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1 MSTTLSSSTYGKDNVKFLKVKKDPQNPKKQEVMEATVTCLLEGGFDTSYTEADNSSIVPT 60

Qy      61 DTVKNTILVLAKTTEIWPIERFAAKLATHFVEKYSHVSGVSVKIVQDRWVKYAVDGKPHD 120
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      61 DTVKNTILVLAKTTEIWPIERFAAKLATHFVEKYSHVSGVSVKIVQDRWVKYAVDGKPHD 120

Qy     121 HSFIHEGGEKRITDLYYKRSGDYKLSSAIKDLTVLKSTGSMFYGYNKCDFTTLQPTTDRI 180
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     121 HSFIHEGGEKRITDLYYKRSGDYKLSSAIKDLTVLKSTGSMFYGYNKCDFTTLQPTTDRI 180

Qy     181 LSTDVDATWVWDNKKIGTVYDIAKAADKGIFDNVYNQAREITLTTFALENSPSVQATMFN 240
           ||||||||||||||||:||||||||||||||||||||||||||||||||||||||||||||
Db     181 LSTDVDATWVWDNKKIGSVYDIAKAADKGIFDNVYNQAREITLTTFALENSPSVQATMFN 240

Qy     241 MATQILEKACSVYSVSYALPNKHYFLIDLKWKGLENDNELFYPSPHPNGLIKCTVVRKEK 300
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     241 MATQILEKACSVYSVSYALPNKHYFLIDLKWKGLENDNELFYPSPHPNGLIKCTVVRKEK 300

Qy     301 TKL 303
           |||
Db     301 TKL 303
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